1.—Recent Advances in the Chemistry of Western Australian Plants

Presidential Address, 1956
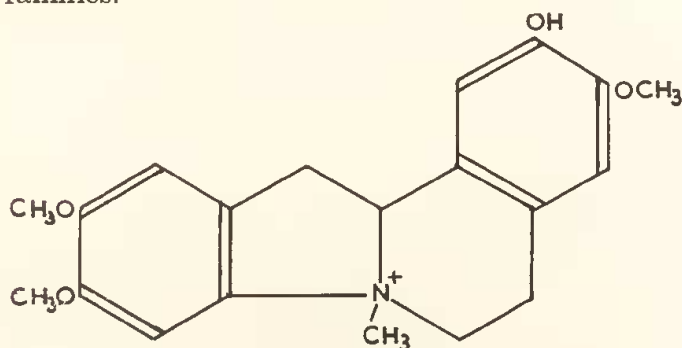
By D. E. White, M.Sc., D.Phil., F.R.A.C.I.*

Delivered 16th July, 1956

Introduction

Twelve years ago, Dr. E. M. Watson (1944) in his Presidential Address to this Society gave us a masterly summary of current knowledge about the chemistry of Western Australian plants. Since that time the investigations initiated by the Drug Panel set up by the Department of Industrial Development of Western Australia (which has now unfortunately lapsed), and by the Australian Phytochemical Survey, which grew from a similar "Drug Plants Survey" in the Eastern States, together with investigations supported by University Research Funds, have added considerably to the knowledge of our native plants. There is still, however, a vast amount of work to be done before we can be said to have explored the chemical potentialities of our flora with anything like thoroughness and I propose to summarise what has been done and to make some observations on what remains to be accomplished.

Rereading Dr. Watson's address, it is somewhat discouraging to see just how many of the promising lines of investigation pointed out by him still remain to be tackled. However, there is some encouragement to be gained from the recommencement of investigations in plant chemistry at the Government Chemical Laboratory and it is to be hoped that these along with investigations in the University and Technical College laboratories will be successful in making a much greater contribution during the next 12 years than I am able to record tonight. Quite substantial progress has been made during the past 12 years in some fields, however. In discussing these I have adopted a primary chemical classification with a sub-classification into plant families.
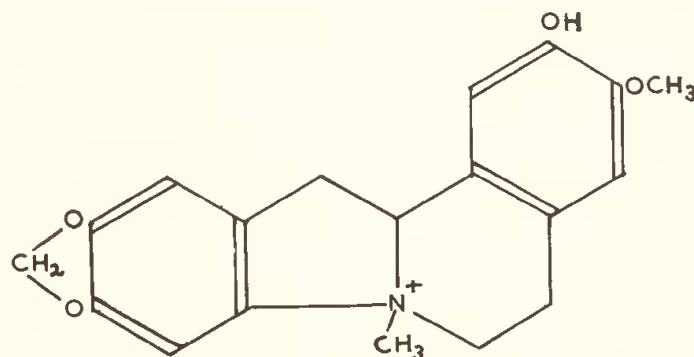
Alkaloids

Lauraceae

This family is represented in Western Australia by *Cryptocarya glaucescens* R. Br. and by several *Cassytha* species.

Although our *Cryptocarya* has not yet been examined some Queensland species have afforded particularly interesting alkaloids, in recent years. These include the first two dibenzopyrrocolines isolated from plants, cryptaustoline (I) and cryptowoline (II) from *C. bowiei* (Hook.)

CRYPTOWOLINE
Fig. II.

Druce (Ewing *et al.* 1953) and the vesicant alkaloid cryptopleurine isolated by de la Lande (1948) from *C. pleurosperma* White et Francis. Chemical study of this alkaloid was difficult and Gellert and Riggs (1954) were only able to establish the presence of a phenanthrene nuclcus and three methoxyl groups.

CRYPTAUSTOLINE
Fig. I.

CRYPTOPLEURINE

Fig. III.

*Chemistry Department, University of Western Australia.

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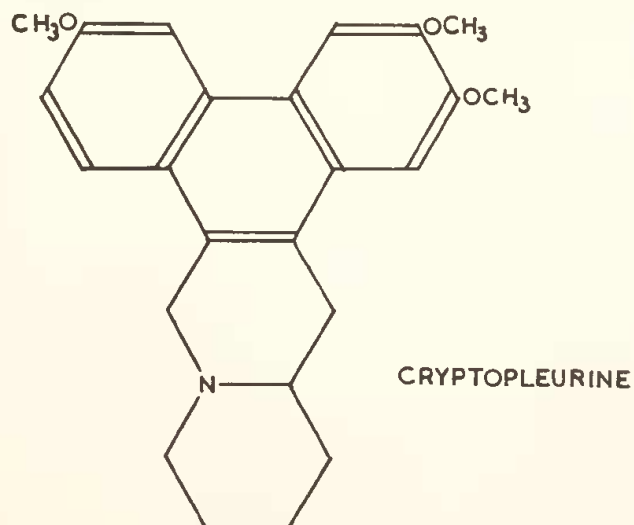
However, the structure of the related *isocrypto-pleurine* methiodide was solved in a very elegant manner by Fridrichsons and Mathieson (1955) by X-ray diffraction studies. This demonstrated that *isocryptopleurine* was a phenanthro-quinolizidine. Gellert (1956) has now shown that *isocryptopleurine* is merely the racemic form of the naturally-occurring alkaloid. Hence this is represented as (III).

Alkaloids of the aporphine group have been reported in *C. triplininervis* R.Br. and *C. angulata* C.T. White (Cooke and Haynes 1954). It will be interesting to see if the Western Australian species is related to either of these three types or if it contains some other type of alkaloid.

One of our *Cassytha* species, *C. pomiformis* Nees has been examined and found to contain 0.04 per cent. of crude alkaloid (Bottomley and White 1949). This genus might well repay closer examination.

Papilionaceae

Several Western Australian *Crotalaria* species have been found to contain substantial quantities of alkaloids. Monocrotaline (IV) was isolated by Adams and Rogers (1939) from *Crotalaria retusa* L. Current investigations (Culvenor 1956) have confirmed this and in addition found other bases and N-oxides in this species and also in *C. mitchelli* Benth. and *C. trifoliastrum* Willd. It has been shown that *C. retusa* is responsible for Kimberley horse disease and may be the sole cause (Gardner 1952; Gardner and Bennetts 1956).
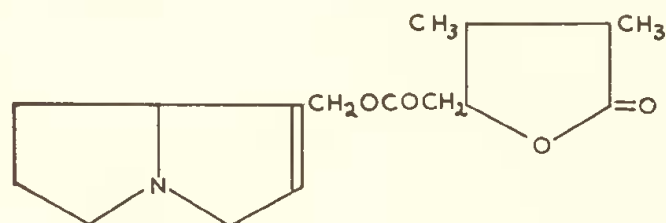
MONOCROTALINE
Fig. IV.
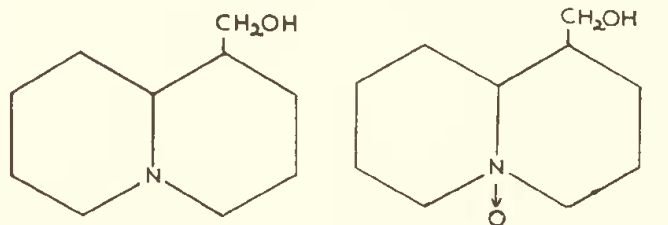
EPILUPININE
Fig. V.

EPILUPININE-N-OXIDE
Fig. VI.

Heavy mortality in sheep grazing on the "Western Australian" blue lupin *(Lupinus varius* L.) during the 1949-1951 seasons led Crow and Riggs (1955) to investigate its alkaloids. They separated four alkaloids by paper chromatography and identified (+) -*epi*lupinine (V), which had been isolated by White (1951) in New Zealand, and also its N-oxide (VI). This was the first recognition of lupinine-N-oxide in nature and is significant because compounds of this type are not isolated by conventional extraction procedures, while they may be re-

sponsible for a substantial part of the toxic effect of the plant. The other alkaloids, which appear to be new, have not yet had their structures determined.

Loganiaceae

The Western Australian *Strychnos lucida* R.Br. is, of course, closely related to the well known *Strychnos nux-vomica,* and is found in Northern Australia from Queensland to the west coast. Earlier work summarised by Webb (1948), indicated the presence of strychnine and brucine in the seeds but Bottomley and White (1947) observed that other alkaloids must be present. Shaw and de la Lande (1948) isolated in addition to strychnine and brucine an amorphous alkaloid which they called lucidine-S. They also obtained an alkaloid named lucidine-L from the leaves. Anet, Hughes and Ritchie (1953) isolated and characterised strychnine and brucine in extracts of the seeds and obtained the glycoside loganin, which had previously been found by Merz and Krebs (1937) in the pulp of *S. nux-vomica* fruits and has since been investigated by Birch and Smith (1956). They found a considerable amount of amorphous alkaloid material in their *S. lucida* seeds and considered that their failure to isolate lucidine-S might have been due to its decomposition in the seeds, which were more than a year old when examined.

Apocynaceae

Alkaloids were isolated from the bark of *Alstonia constricta* F. Muell. over seventy years ago by Hesse (1880). However, it was not until the quinine shortage of World War II forced the examination of every possible alternative, that they were closely studied. Although they did not provide any compounds of value as anti-malarials, the constitution of the major alkaloid, alstonine (VII), was established by Elderfield and Gray (1951), and that of alstoniline by Elderfield and Wythe (1954).
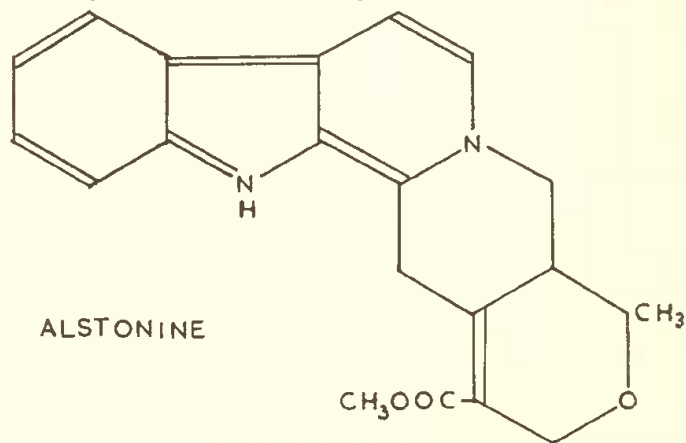
ALSTONINE

Fig. VII.

It was the reported occurrence of alstonine in *Rauwolfia vomitoria* Afzel. and the known botanical relationship of *Alstonia* and *Rauwolfia* species (Crow, 1955) which inspired a reinvestigation of *A. constricta.* As a result Crow and Greet (1955) and Curtis, Handley and Somers (1955) discovered reserpine (VIII) in the root bark. This was an announcement of great importance because of the value of reserpine in the treatment of hypertension and its even greater importance in the treatment of certain

mental disorders. It provides Australia with a convenient native source and makes her independent of the export ban imposed by India and the shortage of supplies from other countries.
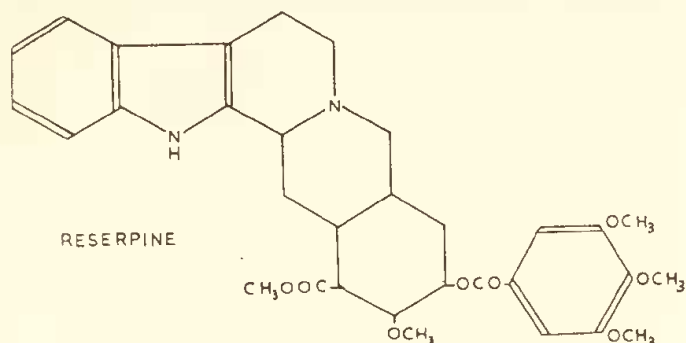
RESERPINE

Fig. VIII.

A thorough examination of the two recorded Western Australian *Alstonia* species deserves immediate attention.

A. actinophylla (A. Cunn.) K. Schum. (= *A. verticillosa* F. Muell.) is known to belong to the non-alstonine-yielding group of Alstonias (Sharpe 1934) but little is known of the constitution of the major alkaloid, echitamine or of the other alkaloids which accompany it, and the Western Australian species might well yield reserpine or some valuable related alkaloid.

Boraginaceae

Heliotropium europaeum L. grows in all the southern Australian states and causes liver damage in sheep, frequently resulting in their death. It has been found by Culvenor, Drum-
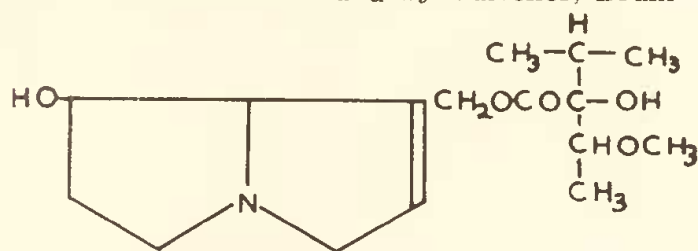
HELIOTRINE

Fig. IX.

mond and Price (1954) to contain five alkaloidal bases and their N-oxides. The two most abundant bases, first isolated by Trautner and Neufeld (1949), were identified as heliotrine
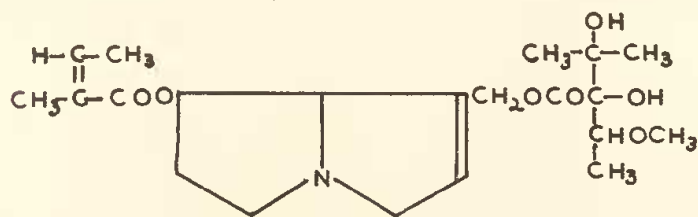
LASIOCARPINE

Fig. X.

(IX) and lasiocarpine (X) previously obtained by Menshikov (1932) from *H. lasiocarpum*. Culvenor (1954) identified the two minor bases as supinine (XI) and supinidine heliotrate and the third major base as heliotridine lasiocarpate.
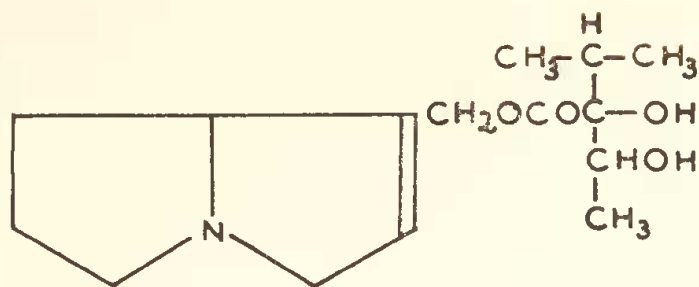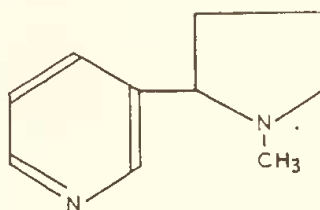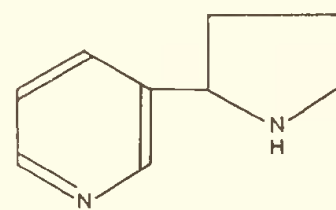
SUPININE

Fig. XI.

Solanaceae

The long-standing controversy about the alkaloids of *Duboisia hopwoodii* (F. Muell.) F. Muell., dating from the isolation of a product named "piturine" (Bancroft, 1872), has now been resolved. The observations of Rothera (1910), who

NICOTINE   NORNICOTINE

Fig. XII.   Fig. XIII.

isolated nicotine (XII), and of Hicks and Le Messurier (1935) and Bowen (1944) who obtained nornicotine (XIII), were reconciled by Bottomley, Nottle and White (1945) who showed that most specimens of *D. hopwoodii* contained both nicotine and nornicotine, but in some nicotine was absent. These observations were confirmed and extended by Bottomley and White (1951b), who obtained samples from four sites (of the 34 examined) which resembled the material examined by Hicks and Bowen in not containing any nicotine.

The alkaloid content, estimated on dried leaves, could not be correlated with locality, season or soil type and an examination of fresh leaves showed that there was a considerable loss of alkaloid on drying. These investigations indicated that *D. hopwoodii* is a much more favourable source of nicotine alkaloids than Hosking (1944) believed but the replacement of nicotine by DDT, gammexane and other insecticides has removed a great deal of the demand for it.

HYOSCINE   HYOSCYAMINE

Fig. XIV.   Fig. XV.

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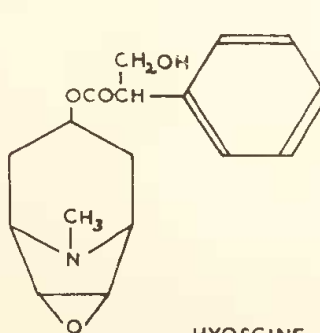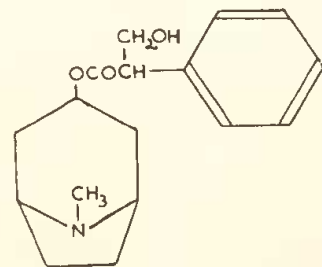
It is remarkable that *Duboisia hopwoodii* differs so strikingly in its alkaloid content from *D. myporoides* R. Br. and *D. leichhardtii* F. Muell which contain the tropane alkaloids hyocine (XIV) and hyoxyamine (XV). These species have now been linked by the observation of Loftus Hills, Bottomley and Mortimer (1953) that *D. myoporoides* grown from seed obtained from New Caledonia contains nicotine and nornicotine as well as hyoscine and hyoscyamine. They suggest that this may be a relic of a primitive form from which the genotypes of the Australian mainland originated.

Compositae

Members of the Compositae which have yielded alkaloids in Australia include *Senecio jacobea* L., which has been studied in Victoria (Bradbury and Culvenor 1954; Bradbury and Willis 1956) because of its known liver-damaging effect on stock.

Western Australian *Senecio* species have not yet been investigated, but *Erechthites quadridentata* D.C. which grows in this state has been found to contain alkaloids of the pyrrolizidine type like *Senecio, Crotalaria,* and *Heliotropium* species. Three alkaloids, senecionine, seneciphylline and retrorsine have been isolated, partly free but mainly as N-oxides (Culvenor and Smith 1955). Like the liver-damaging alkaloids of *Heliotropium europaeum* and the *Crotalaria* and *Senecio* alkaloids they are esters of pyrrolizidine bases.

Non-Alkaloidal Toxic Compounds

Macrozamia spp.

The toxic compound macrozamin was first isolated from the seeds of *Macrozamia spiralis* Miq. by Cooper (1940). Dr. N. V. Riggs obtained the same compound, accompanied by a small amount of sequoyitol for which he proposed the structure (XVI) (Riggs, 1949) from the Western Australian *M. riedlei* (Gaud.) C. A. Gardn. Lythgoe and Riggs (1949) showed that macrozamin was a β-primeveroside of an aglycone $C_2H_5ON_2$
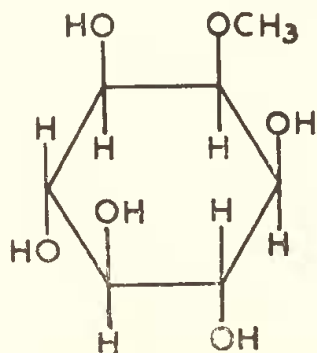
SEQUOYITOL

Fig. XVI.

which contained no readily acetylated grouping and Langley, Lythgoe and Riggs (1951) proposed the two alternative structures (XVII and XVIII). These were substantiated by comparison of its ultraviolet absorption spectrum with the spectra

of synthetic azoxy compounds, but it was not possible to decide between them. Further comparisons with the infrared spectrum of azoxymethane were made by Langley, Lythgoe and Rayner (1952) who studied the acid catalysed decomposition of the synthetic azoxy-com-
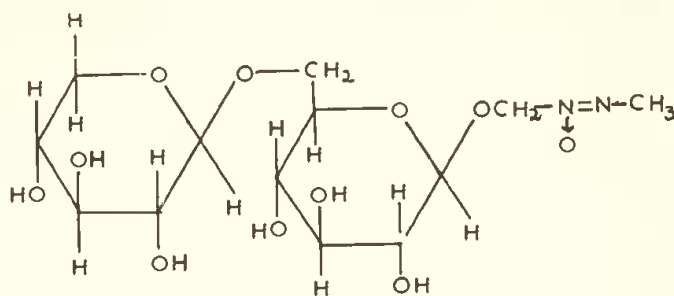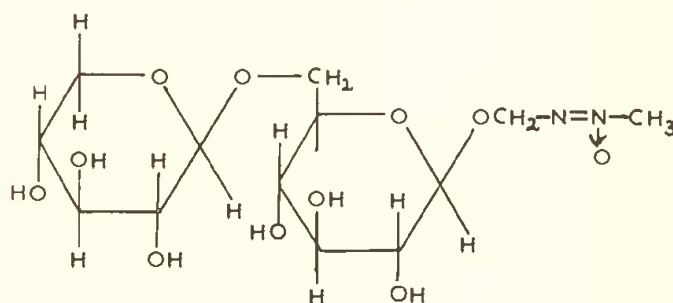

Fig. XVII.

MACROZAMIN

Fig. XVIII.

pounds and concluded that structure (XVIII) was the more likely since the methyl group was oxidised (to formaldehyde) and hydrazine produced, rather than methyl hydrazine. They considered that oxidation would occur at the carbon atom adjacent to the more highly oxidised 4-covalent nitrogen atom.

The same compound has also been obtained by Riggs (1954) from other Cycadaceae including *Cycas, Bowenia* and *Macrozamia* spp. from Queensland, but *M. denisoni* C. Moore seeds did not contain macrozamin or any similar compound.

Oxylobium and Gastrolobium spp.

These two genera provide the largest group of Western Australian poison plants with over thirty toxic members (Gardner and Bennetts, 1956.) In spite of intermittent study over more than 50 years we are still unable to say what is the cause of their toxicity.

They were reinvestigated by Bottomley (1950) who obtained highly toxic concentrates from the seeds of *Oxylobium granticum* S. Moore. However, the small amounts of alkaloids extracted from these were non-toxic and reduction failed to disclose any N-oxides. The water solubility of the toxic material made examinatin by the conventional methods difficult but application of countercurrent extraction and partition chromatography to the extracts should give interesting results and perhaps solve this intriguing problem, which in 1907 was thought to have been solved by the isolation of alkaloids (Mann and Ince, 1907).

Heterocyclic Oxygen Compounds
Genistein

One of the most widely used plants in improved pastures in Western Australia is subterranean clover (*Trifolium subterraneum* L.). Considerable attention was given, therefore, to the demonstration by Bennetts (1944, 1946, 1947) and Bennetts, Underwood and Shier (1946) that it was responsible for poor lambing results and for the loss of many ewes maintained on subterranean clover pastures. Its seriousness is indicated by the fact that lambing may fall below 10 per cent., while loss of ewes may reach 30 per cent., on pastures dominated by the early Dwalganup strain.

Curnow, Robinson and Underwood (1948) showed that the effect was caused by some oestrogenic or oestrogen-producing substance in the plant. Its activity was relatively low as one hundred millionth of a gram of oestradiol would produce a similar effect to one gram of dried clover. However, Curnow (1950) and Beck and Braden (1951) were able to prepare concentrated extracts and demonstrated that the oestrogen was phenolic, although they were unable to purify it completely.
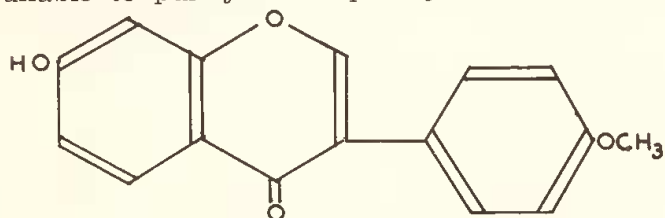
**FORMONONETIN**
Fig. XIX.
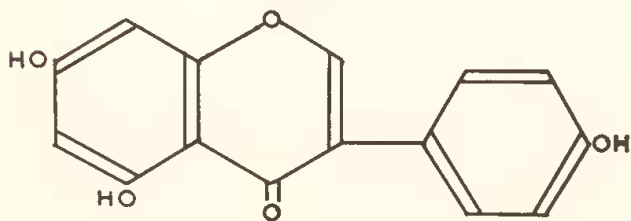
GENISTEIN
Fig. XX.

Bradbury and White (1951) omitted the alkali-treatment used by the previous authors, since this was known to cause decomposition of the oestrogen, isolated from *Butea superba* (Schoeller, Dohrn and Hohlweg, 1940). Using chromatography on alumina to separate compounds from the alcoholic extract, two isoflavones, formononetin (XIX) and genistein (XX) were isolated and genistein was shown to be a weak oestrogen. Biggers and Curnow (1954) estimated that it was between 1/100,000th and 1/16,000th as active as oestradiol depending on the method of administration and showed that it fell into the class designated as pro-oestrogens by Emmens (1941), since it was little more effective when applied directly to the vagina than when injected. This contrasts strongly with the steroid oestrogens which are more than 100 times as effective on local application.

Curnow (1954) showed that the Dwalganup strain of subterranean clover contained more than 0.7 g. of genistein per 100 g. of dry matter and that half of this could be recovered on extraction. From this he concluded that there was sufficient genistein in the plant to account for its oestrogenic activity although he pointed out that treatment with alkali appeared to produce a more active oestrogen.

Meanwhile, it had been shown that some other clovers had similar but less powerful oestrogenic effects and Pope *et al.* (1953) in England isolated a methyl ether of genistein (biochanin-A) from red clover (*Trifolium pratense* L.) and showed that it was weakly oestrogenic. This compound has also been isolated in further studies of alkali-treated extracts of subterranean clover (Beck, Kowala and White, 1956), together with several inactive compounds and probably two other oestrogens, which have not yet been obtained in sufficient quantity to enable their constitutions to be determined, but which are much more active than genistein. Even if they are artefacts these compounds may indicate the structural type of the true oestrogen formed from genistein in the animal body. In this connection the synthetic oestrogens prepared by Bradbury and White (1953) and by Bradbury (1953) are also of interest.
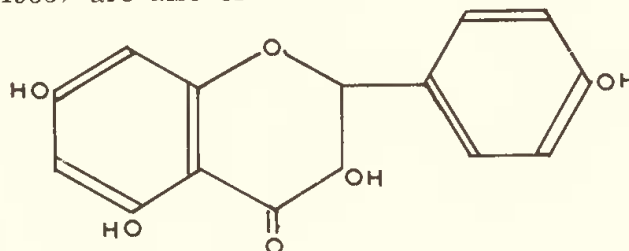
**AROMADENDRIN**
Fig. XXI.

Aromadendrin

The red kino exuded from the bark of *Eucalyptus calophylla* R. Br. is responsible for its common name "Redgum" and from this kino H. G. Smith (1896) isolated a colourless crystalline compound which he called aromadendrin. Its structure has now been determined as a dihydrokaempferol (XXI; Hillis, 1952.) Hillis has found this compound in a large number of eucalypt kinos, and overseas investigators have found it and related compounds in a variety of plants (references quoted by Hillis, 1952; Gripenberg, 1952; Tominaga, 1953.) It seems that compounds like this may form with the flavones, flavonols, leucoanthocyanidins, anthocyanidins and catechin-like compounds a complex oxidation-reduction system which might be of profound importance in plant metabolism.

Vellein

The toxicity of *Velleia discophora* F. Muell. (Goodeniaceae) to stock (Gardner and Bennetts, 1956) led to its chemical examination. Bottomley and White (1951a) isolated from it the glycoside vellein, which they identified as the β-glucoside of osthenol (XXII). This

structure was confirmed by synthesis of tetraacetylvellein from O-tetraacetyl-α-gluco-sidyl bromide and osthenol.
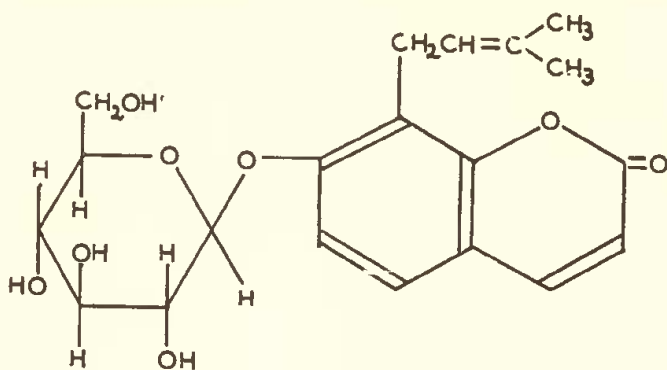
VELLEIN
Fig. XXII.

Vellein is accompanied by a smaller amount of another coumarin named discophoridin (Bottomley, 1950), the structure of which has not been elucidated.

Neither of these compounds has yet been subjected to pharmacological testing.

Essential Oils

The essential oils of Australian plants attracted attention from the time of the first settlement in New South Wales, when the Surgeon to the First Fleet, Dr. White, distilled the oil from *Eucalyptus piperita* Sm. and noted its peppermint odour. H. G. Smith was largely responsible for the systematic examination of many of these oils and extended his collections to Western Australia. Subsequently many chemists in Australia and overseas have contributed to this field which was until a few years ago the only one in which a really substantial amount of work on Australian plant chemistry had been accomplished.

However, the investigation of the oils of Western Australian plants has not been nearly as extensive nor as thorough as could be wished and there are many large gaps in our knowledge.

Coniferae

No new chemical investigations of Western Australian members of this family have been reported since Watson's summary (1944) with the exception of the publication of Murray's observations (1950) on the leaf oil of *Callitris Morrisoni* R. T. Baker, the major constituents of which are pinene and limonene.

With the recognition of the 7-membered ring tropolones in overseas members of the Coniferae it would seem well worthwhile to reinvestigate the wood-oils of our species. Interest has also been added by a recent report of the presence of tumor-damaging compounds in extracts of *Podocarpus* and *Callitris* spp. (Hartwell 1956).

Santalaceae

The most important contribution to the chemistry of this family has been the elucidation of the structure of the sesquiterpene alcohol lanceol

which occurs in *Santalum lanceolatum* R. Br. Bradfield *et al.* (1936) proposed a unique 5-membered ring structure (XXIII) for this compound but it has now been shown to be related to the known monocyclic sesquiterpene bisabolene (Birch and Murray 1951; Eschenmoser, Schreiber and Keller 1951). It probably has one of the two structures (XXIV) or (XXV) although Eschenmoser, Schreiber and Keller also consider an 8-membered ring possible.
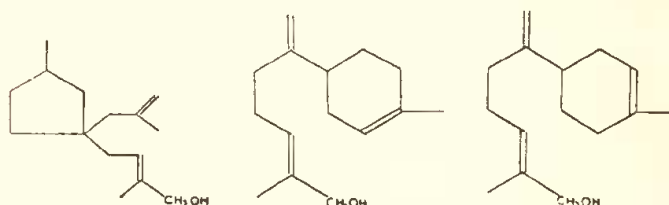

Fig. XXIII.   Fig. XXIV.   Fig. XXV.

It has also been shown (Birch, Mostyn and Penfold, 1953) that the oil of *Santalum spicatum* R. Br. *(Eucarya spicata* Sprague et Summ.) contains in addition to the α- and β-santalols recognised by Penfold (1928, 1932) the open-chain sesquiterpene alcohol farnesol. This explains previous observations that the sesquiterpene alcohol fractions often had a lower density refractive index and optical rotation than would be expected from a mixture of α- and β-santalols.

Phytolaccaceae

The essential oil of *Codonocarpus cotinifolius* (Desf.) F. Muell. was investigated by Bottomley and White (1950a) and (+)-secbutyl-*iso*thiocyanate and benzyl cyanide were identified in it. Both compounds are probably derived from mustard oil glycosides in the plant.

Rutaceae

Murray's observations (1939) on the leaf-oil of *Phebalium filifolium* Turcz. have been published (1950). It contains a substantial amount of hydrocarbon, which may be sabinene. Preliminary investigation (Bottomley and White, 1947) of the leaf oil of *P. drummondii* Benth. var. *bullatum* (J. M. Black) C. A. Gardn showed that it was of quite different type, containing mainly esters. Essential oils have been distilled from small samples of six other Western Australian plants belonging to this family *(Boronia, Eriostemon* and *Phebalium* spp.; Bottomley and White 1949) but they have not yet been examined in detail.

Myrtaceae

The oils obtained from three varieties of *Eucalyptus oleosa* F. Muell. ex Miq. have been described by Gardner and Watson (1948). These all give excellent yields of steam-volatile oils (see Table) with very high cineole contents. Of the 85 specimens examined only two specimens of var. *borealis* had less then 80% cineole. The var. *plenissima* particularly should be well worth cultivating commercially for its oil, especially in view of the fact that it thrives in the low rainfall areas on the eastern margin of the wheat belt.

TABLE I
Oils from *Eucalyptus oleosa* vars.

Variety	No. of Speci-mens	Yield (%)		Cineole (%)	
		Range	Average	Range	Average
borealis C. A. Gardn.	13	2·1–4·7	3·0	72·8–92·8	86·1
kochii C. A. Gardn.	23	2·3–5·5	3·5	82·7–93·8	84·8
plenissima C.A. Gardn.	49	2·2–8·6	4·2	83·0–94·8	89·5

The bark of an Eastern Goldfields eucalypt reported as *E. eudesmioides* F. Muell., but which we have since learned was *E. gongylocarpa* Blakely was found by Blumann, Michael and White (1953) to contain cineole, borneol and the crystalline sesquiterpene alcohol globulol. This compound was of special interest because following the original reports of its occurrence in *E. globulus* oil residues (Schimmel & Co. 1904; Semmler and Tobias 1913), Ruzicka, Pontalti and Balas (1923) had been unable to obtain it crystalline, but concluded that unlike any other known *Eucalyptus* oil constituent, it was a derivative of cadalene.
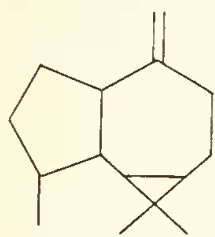

AROMADENDRENE
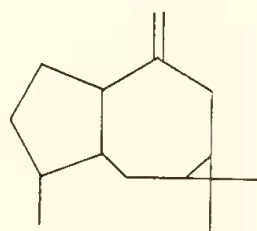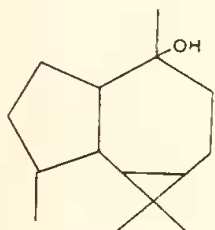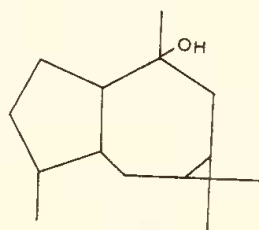Fig. XXVI.   Fig. XXVII.

GLOBULOL
Fig. XXVIII.   Fig. XXIX.

It has now been possible (Blumann *et al.* 1954) to show that in fact globulol is related to the common eucalpyt sesquiterpene aromadendrene and that like the sesquiterpene alcohol, guaiol, which is found in *Callitris* timbers, it is an azulene derivative. Taken in conpunction with Birch and Lahey's (1953) suggested structures for aromadendrene (XXVI and XXVII) two possible structures have been proposed for globulol (XXVIII and XXIX).

An examination of the essential oils of three Western Australian *Melaleuca* species carried out by Murray (1939) and already discussed by Watson (1944) has now been published (Murray, 1950). Watson (1944) noted that essential oils had not yet been distilled from 100 of our *Eucalpytus* spp., 94 of our *Melaleuca* spp. and most of the other oil-yielding genera of Myrtaceae which occur in Western Australia. Since then oils have been distilled from 12 species belonging to the genera *Balaustion,*

Chamaelaucium, Darwinia, Hypocalymma, Melaleuca, Micromyrtus and *Thryptomene* (Bottomley and White, 1949) but lack of research workers has halted progress at this stage. I believe that it will be possible to take up these investigations again in the near future and I trust that the project will receive sufficient support to enable the vigorous prosecution of the work. The results should be of considerable interest, not only to research scientists but also to progressive industrialists and deserve to be supported and encouraged.
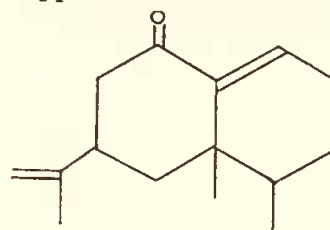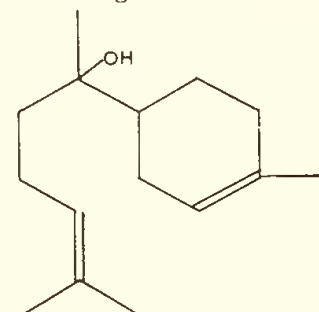

EREMOPHILONE
Fig. XXX.
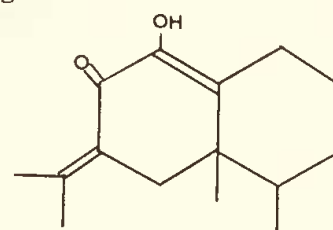
HYDROXYEREMOPHILONE
Fig. XXXI.
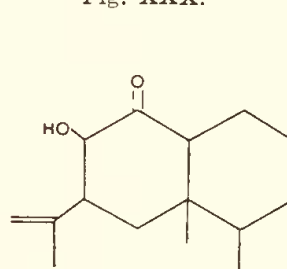
HYDROXYDIHYDROEREMOPHILONE
Fig. XXXII.

ANYMOL
Fig. XXXIII.

Myoporaceae

This family attracted attention when the Eastern Australian *Eremophila mitchellii* Benth. was reported to contain three sesquiterpene ketones (Bradfield, Penfold and Simonsen 1932) which proved to be of unusual skeletal type (XXX, XXXI and XXXII; Gillam *et al.* 1941). More recently a sesquiterpene alcohol of more normal type named anymol (XXXIII) and found to be one of the stereoisomers of bisabolol has been isolated from *Myoporum crassifolium* Forst. from New Caledonia (O'Brien *et al.* 1954) while the toxic ketone ngaione (XXXIV), first reported in *M. laetum* Forst. f. (Cunningham and Hopkirk 1945) has also been found in some specimens of *M. acuminatum* R. Br. (Birch, Massy-Westropp and Wright 1953).

NGAIONE
Fig. XXXIV.

7
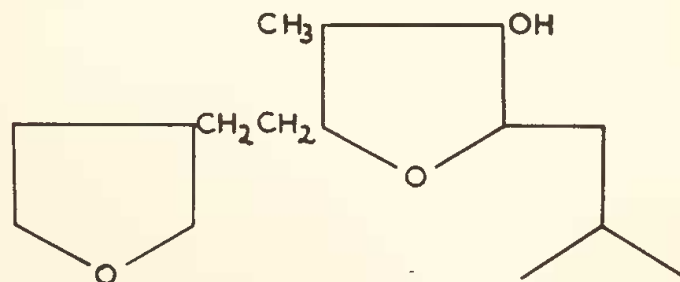
No further work on the oils of Western Australian species has been published since Watson's summary (1944) in spite of the fact that several *Eremophila* and *Myoporum* species are either known or suspected to be toxic to stock.

Polyterpenoids
Pittosporaceae

Pittosporum undulatum Vent. was examined by Cornforth and Earl (1938) who isolated a triterpenoid sapogenin which they named pittosapogenin and formulated as $C_{30}H_{50}O_7$. Repetition of this work on material from plants cultivated in Western Australia yielded some of the same compound, which however proved to be a hexahydroxy-compound $C_{30}H_{50}O_6$ and was accompanied by larger amounts of a pentahydroxy compound $C_{30}H_{50}O_5$ which proved to be identical with A_1-barrigenol, obtained by Nozoe (1935) from *Barringtonia asiatica* Kurz. The constitution of the latter compound (XXXV) has recently been established (Cole *et al.* 1955) and work on the structure of pittosapogenin is proceeding.
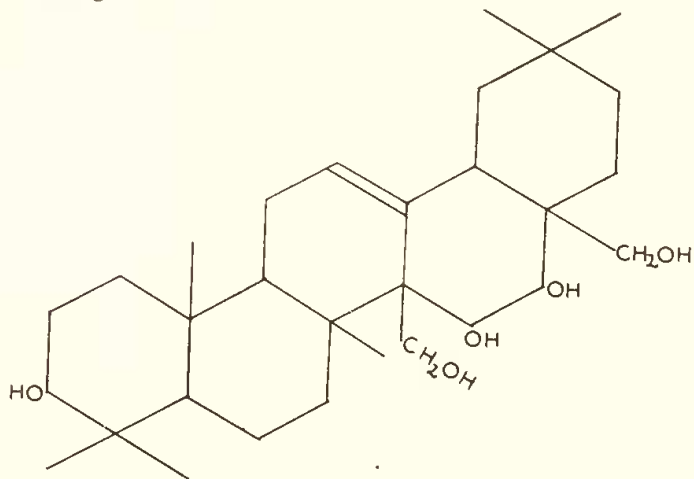
A₁-BARRIGENOL
Fig. XXXV.

From the Western Australian species *P. phillyracoides* D.C., pittosapogenin has also been isolated, but in this plant it is accompanied by a compound containing only 4 oxygen atoms ($C_{30}H_{48}O_4$) which has been named phillyrigenin. This has been shown to have a primary and a secondary hydroxyl group and a six-membered lactone ring (Beckwith *et al.* 1956). Further investigations on its constitution are proceeding and investigations on other members of this family are proposed.

Euphorbiaceae

Although *Euphorbia* spp. commonly contain tetracyclic triterpenoids (Gascoigne 1955; Halsall 1955) and a hexacyclic triterpenoid has been isolated from *Phyllanthus engleri* Pax (Alberman and Kipping 1951; Barton, Page and Warnhoff 1954), *Petalostigma sericea* (R. Br.) C.A. Gardn. has been found to contain the common pentacyclic oleanolic acid in the fruits. On the other hand *Beyeria leschenaultii* (D.C.) Bail. var. *drummondii* Muell. Arg. afforded a trihydroxy diterpenoid, which has been named beyerol (Jefferies 1950). Its constitution is under in-

vestigation and it is hoped to be able to report on its structure in the near future.

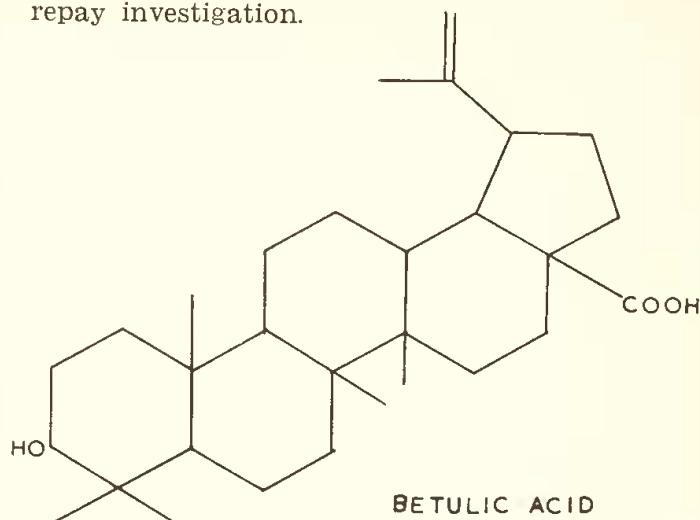Other members of this family may very well repay investigation.

BETULIC ACID
Fig. XXXVI.

Loranthaceae

The Christmas tree, *Nuytsia floribunda* (Labill.) R. Br. has been reported to contain a milky fluid (Herbert 1919) and examination of the alcoholic extract of leaves and stems revealed the presence of betulic acid (XXXVI) and a little betulin (Anstee *et al.* 1952). Betulin is a well known constituent of birch barks, and betulic acid had previously been found in one Australian and several overseas plants (*cf.* Ralph and White 1949).

Myrtaceae

The bark of *Eucalyptus calophylla* R. Br. afforded the acetate of the well-known oleanolic acid (White and Zampatti 1952) but six *Melaleuca* spp. (*M. rhaphiophylla* Schau., *M. cuticularis* Labill., *M. viminca* Lindl., *M. leucadendron* L., *M. parviflora* Lindl., and *M. pubescens* Schau.) all yielded betulic acid in the insoluble sodium salt fraction (Anstee *et al.* 1952). The first five of these species are "paper-barks" and crystalline triterpene acid can be seen in places between the papery layers of the bark. The compound isolated from *M. leucadendron* by Isii and Osima (1939) and called "melaleucin" is probably impure betulic acid.
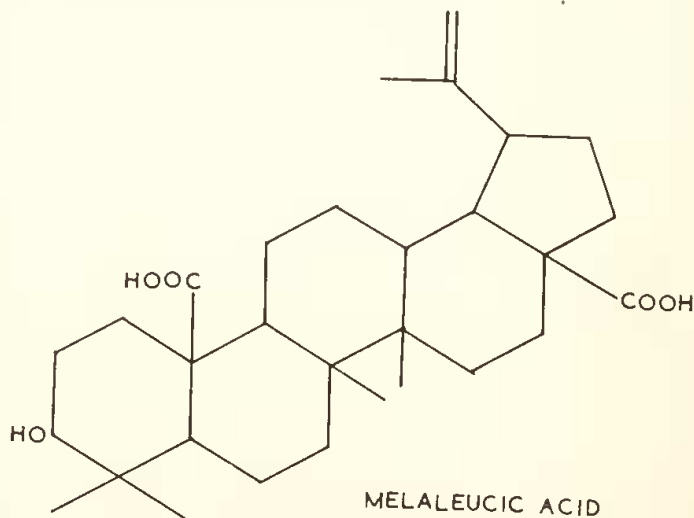

MELALEUCIC ACID
Fig. XXXVII.

In addition three species, *M. rhaphiophylla,* *M. cuticularis* and *M. viminea* contain a second triterpene acid, which has beeen named melaleucic acid. It has been shown to be closely related to betulic acid and is particularly interesting as only the second triterpenoid dicarboxylic acid to have its structure established (XXXVII; Arthur *et al.* 1956).

Apocynaceae

Alyxia buxiofolia. R. Br. proved somewhat unusual in that material collected at Kalgoorlie contained betulic acid, but when we attempted to isolate more betulic acid from plants collected from Point Peron we obtained a mixture of oleanolic and ursolic acids (Anstee *et al.*, 1952). This observation agrees well with the suggestion that the pentacyclic triterpenoids of the oleanane, ursane, lupane (betulic acid) and taraxastane series all arise from a common precursor (Dietrich and Jeger, 1950) as well as with the more general derivation from squalene (Eschenmoser *et al.*, 1955).
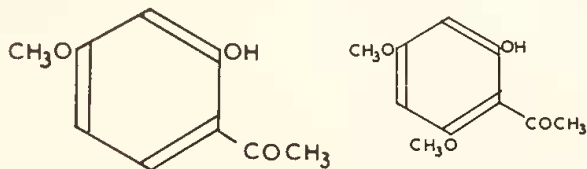
Solanaceae

Ursolic acid has been isolated from *Duboisia hopwoodii* (F. Muell) F. Muell (Trautner and Neufeld, 1947; Bottomley and White, 1951b) from *Anthotroche blackii* F. Muell and *Anthotroche pannosa* Endl. (Bottomley and White, 1950b) and it is also found together with oleanolic acid in *Anthoceris littorea* Labill. and *Anthocercis odgersii* F. Muell. while the triterpene acid mixture in *Anthocercis intricata* F. Muell. is probably similar (Anstee *et al.*, 1952).

Other Compounds
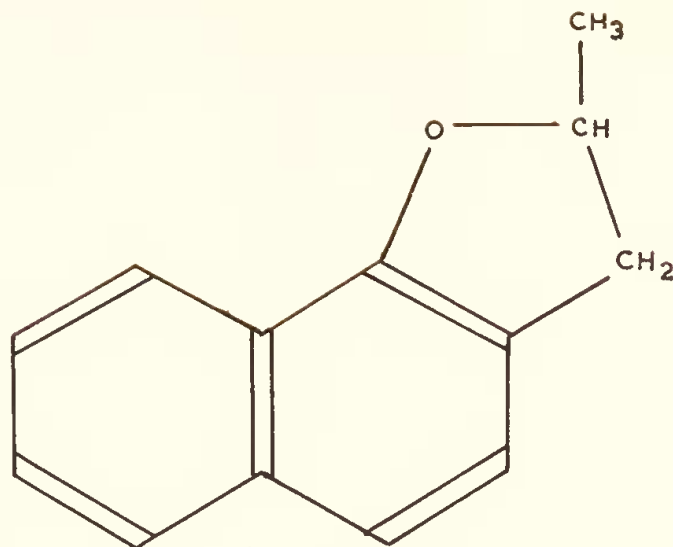### *Xanthorrhoea Resins*

The resins of the "blackboys" (*Xanthorrhoea* spp.) so characteristic of the Western Australian scene have engaged the attention of chemists for many years. Rennie, Cooke and Finlayson (1920) and Finlayson (1926) by steam distillation of an alkaline solution of the resin obtained paeonol (XXXVIII). It was accompanied by another crystalline compound which they called "hydroxypaeonol." Birch and Hextall (1955) have recently shown that this is, in fact, 2-hydroxy-4 : 6-dimethoxy-acetophenone (XXXIX), and have identified their xanthorrhoein as a naphthalene derivative, possibly (XL).

XANTHORRHOEIN
Fig. XL.

2′:4 –DIHYDROXY– 4′–METHOXYCHALKONE
Fig. XLI.

Duewell also showed that bushfire-damaged resin yielded chrysophanic acid (1 : 8-dihydroxy-3-methylanthraquinone) and showed that this compond was produced by fire treatment. It would be interesting to know what compound in the original resin is responsible for its formation.

Future Work

It is clear from the foregoing discussion that there is no lack of problems for investigation now and in the foreseeable future.

The alkaloid field does not look particularly inviting since the alkaloid contents of our dry-country plants appear to be low, but there are still numerous plants worthy of investigation. *Anthocercis littorea* alkaloids deserve further investigation while *A. viscosa* R. Br. and some of the other species of this genus may be more interesting. Our *Senecio* and *Erechthites* spp. should be of interest in extension of the work by C.S.I.R.O. in this group of plants, whilst there are numerous *Solanum* species available in this State which should be well worthy of close study since they might provide compounds of value in the synthesis of cortisone.

Toxic plants provide many possible problems of great potential interest. There are over thirty toxic *Gastrolobium* and *Oxylobium* species alone (Garden and Bennetts, 1956) while *Stypandra, Homeria, Myoporum* and *Eremophila* are obvious choices for early investigation.
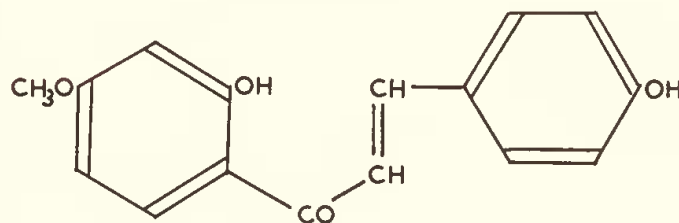

PAEONOL
Fig. XXXVIII.

2-HYDROXY-4:6 –DIMETHOXY ACETOPHENONE
Fig. XXXIX.

Duewell (1954) suggested that paeonol might arise by alkaline decomposition of 2′ : 4-dihydroxy-4′-methoxychalkone (XLI), which he isolated from *X. australis* R. Br. The same decomposition would also afford *p*-hydroxybenzaldehyde which was isolated from the resin by Bamberger (1893), while 2-hydroxy-4 : 6-dimethoxyacetophenone could well be derived from a closely related compound.

9

The lack of knowledge of our essential oils, I have already stressed, while the investigation of the polyterpenoid constituents of genera like *Bassia* (Chenopodiaceae), *Phyllanthus* (Euphorbiaceae) and other members of the Euphorbiaceae and the Pittosporaceae are particularly likely to yield interesting results.

All such investigations are in fact long-term projects. Even if a team of half-a-dozen workers could be put to work in each of the fields I have indicated it is unlikely that they would produce substantial results in less than three or four years and it might take twenty years to solve some of the problems but I do feel that we should be tackling the problem of investigating our native plants on some such scale as this. I believe that our group at the University has given some idea of what can be accomplished by a small group which in the early years especially was sadly lacking in experience. In spite of this and many other commitments we have published a dozen papers dealing with twenty different plants in the past 11 years. Let us set out to build onto this so that in another 30 years we will have multiplied this effort by at least twelve and we can say that most of the known problems of interest and importance are at least under investigation if not already solved.

Perhaps it is too much to hope for this in the light of our rate of progress to date. However, I feel that if we can enlist the whole-hearted support of the farmer and the pastoralist to finance work on toxic plants and of the industrial community to support investigations on alkaloids, essential oils and polyterpenoids, all of which are of potential industrial importance, then we can attract research workers by the provision of well paid posts with reasonable security. If we are successful in this we should be able to say, at least in 50 years from now, "We know the more important constituents of our common plants and we are making the best possible use of them in the interests of the community." When we can do this, I will feel that I have achieved my object in drawing your attention to these problems and enlisting your support for a vigorous effort towards their solution.

Acknowledgments

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